

REMARKS

After entry of this amendment, claims 1-9, 11-13, 15-25, and 27-33 are pending; claims 30-33 are new and supported by original claims 1-4. Claims 10, 14 and 26 were previously canceled.

35 U.S.C. § 112 Rejection

Reconsideration is respectfully requested of the rejection of claims 2-3, 5-9, and 23-24 under 35 U.S.C. § 112, second paragraph as failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claims 2-3, 5-9, and 23-24

Claims 1 and 22 are independent and merely require "a patient exposed to radiation for a time and at an intensity sufficient to result in alopecia." This claim element modifies radiation and describes its time and intensity and requires that it be sufficient to result in alopecia. In this context, the word "exposed" is passive. The passive voice is useful "when it is more important to draw attention to the person or thing acted upon."¹ In claims 1 and 22, it is important to draw attention to the patient that is being treated and thus, the broadest interpretation of this claim element is that the passive "exposed" encompasses all the passive tenses including the present tense (is exposed), the present perfect tense (has been exposed), the past tense (was exposed), the past perfect tense (had been exposed), the future tense (will be exposed), the future perfect tense (will have been exposed), the present progressive tense (is being exposed), and the past progressive tense (was being exposed). Therefore, this description of the radiation treatment does not require any temporal relationship between administration of the methionine protectant agent and the radiation exposure.

Further, under the principle of claim differentiation, two claims in the same patent will not have identical scope, but instead, will have an intended difference in scope. With this in mind, the claim structure makes it clear that claims 1 and 22 were intended to include all temporal relationships between administration methionine

¹ <http://grammar.ccc.commnet.edu/grammar/passive.htm>

protectant agent and radiation exposure. Thus, claims 1 and 22 include administration of the methionine protectant agent prior to (claims 2 and 23), simultaneously with (claims 3 and 24) and after (claims 4 and 25) exposure to radiation and accordingly, claims 2-3, 5-9, and 23-24 satisfy the requirements of 35 U.S.C. § 112.

Claims 31 and 32

To expedite prosecution, new claim 30 has been added and it requires "exposing the patient to radiation for a time and at an intensity sufficient to result in alopecia." Because this radiation exposure requirement does not indicate that the radiation exposure occurs before or after administration of the methionine protectant agent, claim 30 neither requires nor suggests a temporal relationship between administration of the methionine protectant agent and the radiation exposure. Further, under the principle of claim differentiation, claim 30 is interpreted to include the administration of the methionine protectant agent before (claim 31), simultaneously with (claim 32) or after (claim 33) radiation exposure. Thus, new claims 31 and 32 satisfy the requirements of 35 U.S.C. § 112, second paragraph.

35 U.S.C. § 103 Rejection

Reconsideration is respectfully requested of the rejection of claims 1, 4, 11-13, 15-22, 25, and 27-29 under 35 U.S.C. § 103 as being unpatentable over Dye (U.S. Patent No. 5,122,369) in view of Jacobs et al. (Treatment of Radiation-Induced Alopecia, Head Neck Surg, 1979, 2(2), 154-159, abstract only).

The Dye reference relates to natural hair loss, not hair loss caused by treatment with radiation. For treating natural hair loss, Dye generally discloses various compositions comprising divalent iron and pantothenic acid along with racemic d,l-methionine. The reference also describes the stages of natural hair follicle growth and loss and relates the follicle stages to calcium concentration. For example, there are three phases in the natural hair loss cycle. The anagen phase is associated with active growth and high metabolic activity in the bulb region, the catagen phase is a transitory phase where the metabolic activity slows, and the telogen phase corresponds to a rest period followed by the hair follicle

being pushed out by a new anagen hair. Dye described this three phase pilar cycle as depending on nutritional, endocrinal, and nervous (e.g., stress) factors.

According to Dye, the calcium concentration in the bulb of the hair generally increases across these stages, with the calcium concentration lowest in the anagen stage bulbs and highest in the telogen stage bulbs. Dye further states that "[t]hese observations have led to the development of a composition that has at least one active ingredient consisting essentially of active chelating agents"² and "the ability of such compositions to chelate divalent calcium ions is generally credited to be responsible for their efficacy."³ The mechanism of hair loss described by Dye implies that by chelating or otherwise reducing the calcium concentration in the hair follicles, the natural progression to the telogen phase can be slowed or arrested. Generally, as Dye describes, follicles with higher calcium concentrations are closer to being lost.

However, the Examiner has not cited any reference that would provide a reason that a person of skill would have believed that hair loss from causes other than the natural pilar cycle would also exhibit a similar calcium concentration profile. More particularly, there is no suggestion in Dye, or other art of record, that radiation would generate excessive calcium in the follicle bulbs.

Jacobs et al. is directed to treatment of radiation-induced alopecia through a punch graft hair transplantation technique. While the abstract does state that radiation alopecia is a well-known complication of high-dosage radiotherapy, the abstract as a whole would have led a skilled person to conclude that hair transplantation was the best treatment approach.

Further, contrary to the Office's assertion, neither Dye nor Jacobs provides a reason to combine the disclosures. The Examination Guidelines for Determining Obviousness in view of *KSR International Co. v. Teleflex Inc.* states that

[t]he key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious...there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.⁴

² See Patent No. 5,122,369, column 2, lines 30-32.

³ See Patent No. 5,122,369, column 2, lines 32-34.

⁴ See Fed. Reg., 72(195), October 10, 2007, page 57526, 57528-57529.

The Office has not provided articulated reasoning with some rational underpinning as to why the artisan would have found the claimed invention to have been obvious. To the contrary, the Office's assertion picks the portion of the Jacobs abstract that states that alopecia is a well-known complication of high-dosage radiotherapy, but fails to mention that the abstract proposes a surgical hair transplantation solution to this problem. Thus, the Jacobs abstract as a whole would have led a person of skill in the art away from a chemical solution to radiation-induced alopecia. Further, Dye does not provide any reason that a skilled person would have believed that calcium levels would be affected by radiation or that controlling the calcium concentration in the hair follicles would affect radiation-induced alopecia. Thus, contrary to the Office's assertion, there would not have been a reasonable expectation that the Dye composition would be effective as a protectant for alopecia arising from radiation exposure as required by claims 1 and 22.

In further support of this conclusion, various prior art references would have led those skilled in the art to investigate the effect of ionizing radiation on cell DNA, and perhaps the influence of protein p53 on cell apoptosis - and not the effect of calcium - in identifying the cause of radiation-induced alopecia and/or possible remedies for this condition. For example, Hutchinson⁵ describes that DNA is the target of ionizing radiation and that death of cells results when cells cannot repair their damaged DNA. The damaging of DNA by radiation and the lack of repair does not depend on the calcium concentration. Further, various references⁶ describe protein p53 as playing a central role in radiation responses, including cell growth arrest and apoptosis. Additionally, other references⁷ describe the regulation by p53 of various genes that are believed to mediate cell cycle arrest. The Examiner has not cited any reference that suggests the genesis or function of protein p53 depends on the calcium concentration, or that the process of apoptosis otherwise implicates the concentration of calcium in the cell or its environment. The references described above were all published well before the priority date of this application and are therefore entitled

⁵ Hutchinson, *Cancer Res.* **1966**, 26, 2045.

⁶ Kastan et al., *Cell* **1992**, 71, 587; Kuerbitz et al., *Proc Natl Acad Sci USA*, **1992**, 89, 7491; Canman et al. *Cold Spring Harbor Symposia on Quantitative Biology*, **1994**, 59, 277; Levine, *Cell* **1997**, 88, 323.

⁷ Midgley et al., *J. Cell Sci.* **1995**, 108, 1843; MacCallum et al., *Oncogene* **1996**, 13, 2575; McDonald et al., *Cancer Res.* **1996**, 56, 2250; Brugarolas et al., *Nature* **1995**, 377, 552; Deng et al., *Cell* **1995**, 82, 675.

to consideration in evaluating obviousness against the entire background of the art⁸. Thus, a person of ordinary skill would have contemplated the mechanisms described above as the causes of radiation-induced alopecia.

Therefore, claims 1, 4, 11-13, 15-22, 25, and 27-29 are patentable over Dye (U.S. Patent No. 5,122,369) in view of Jacobs et al. (Treatment of Radiation-Induced Alopecia, Head Neck Surg, 1979, 2(2), 154-159, abstract only).

The Claimed Methods are Not *prima facie* Obvious in View of the Claims of the Cited Patents.

The analysis employed in an obvious-type double patenting rejection parallels the guidelines of a 35 U.S.C. § 103 obviousness determination.⁹ However, an important distinction exists. A rejection for obviousness must be based on a comparison of the claimed invention to the entirety of the disclosure in the prior art reference, whereas an obviousness-type double patenting rejection must be grounded on a comparison of the claimed invention to the claims, **and only the claims**, of the reference.¹⁰

U.S. Patent Application No. 11/539,975

Claims 1-9 and 11-29 of the instant application are directed to methods for treating alopecia in a patient exposed to radiation, the method comprising administering to said patient an effective amount of a methionine protective agent. Claim 17 of the '975 application is directed to the use of a combination that can include a methionine protectant agent for a variety of insults. The methionine protectant agent of the '975 claims comprises at least two protectant agents wherein one of these agents can be a methionine protectant agent. Claim 17 of the '975 application would not have suggested the instant claims because none of the claim elements would have lead an ordinary person to select alopecia and radiation from the universe of toxicities and insults claimed.

⁸ *In re Kuderna*, 165 USPQ 575 (CCPA 1970).

⁹ *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991).

¹⁰ *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 98 F.Supp.2d 362, 392, 55 USPQ2d 1168, 1190 (S.D.N.Y. 2000), *aff'd*, 237 F.3d 1359, 57 USPQ2d 1647 (Fed. Cir. 2001).

Further, the filing date of the '975 application is October 10, 2006, while the filing date of the instant application is October 27, 2003. Therefore, since the filing date of the instant application is earlier, once the instant application is otherwise in condition for allowance, this double patenting rejection should be withdrawn because the instant application is earlier filed.¹¹

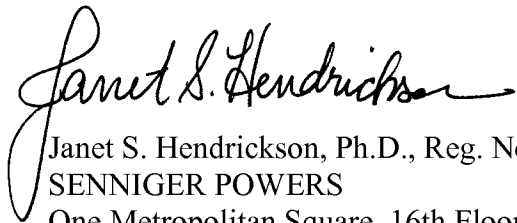
¹¹ M.P.E.P. § 804.

CONCLUSION

Applicant submits that the present application is in condition for allowance and requests early allowance of the pending claims.

The Commissioner is hereby authorized to charge any underpayment and credit any overpayment of government fees to Deposit Account No. 19-1345.

Respectfully submitted,

A handwritten signature in black ink, reading "Janet S. Hendrickson". The signature is fluid and cursive, with a long horizontal flourish extending to the right.

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